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| 09/027,671 | 02/23/1998 | ALAN K. SMITH | 4292-0048-55 | 3507 |
| 22850 | 7590 | 08/18/2004 | EXAMINER | |
| OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C. | | | SAUNDERS, DAVID A | |
| 1940 DUKE STREET | | | ART UNIT | |
| ALEXANDRIA, VA 22314 | | | PAPER NUMBER | |
| | | | 1644 | |

DATE MAILED: 08/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

027,671

Applicant(s)

SMITH et al

Examiner

SAUNDERS

Group Art Unit

1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 5/24/04
- ☒ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 6-7, 10-12, 38-41, 49-69 is/are pending in the application.
- ☐ Of the above claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 6-7, 10-12, 38-41, 49-69 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
 - ☐ received in Application No. (Series Code/Serial Number) _____
 - ☐ received in this national stage application from the International Bureau (PCT Rule 1.7.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☒ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Interview Summary, PTO-413
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Other _____

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The amendment of 5/24/04 has been entered. Claims 6-7, 10-12, 38-41 and 49-69 are pending and under examination.

The following corrections apply to the office action of 12/23/03:

At page 2, line 9 "obliviously" should be – previously.

At page 4, line 1 "record in" should be – record. In --.

At page 4, line 2 "disclosure He" should be – disclosure, he--.

At page 4, third line from bottom, "6-12" should read as –6-8, 10-12--.

The amendment has overcome the following bases of rejection stated in the office action of 12/23/03:

The 112, 2nd rejection of claims 39 and 45.

The 112, 1st rejection of claim 42.

The 102 rejection over Freedman et al. The taught medium exchange rates are in excess of what is recited in instant claim 38.

The 102 rejection over Schneider et al in light of Kuada et al. Schneider et al teach a medium exchange rate of 40%, which is outside the limits of instant claim 38.

Claims 6-7, 10-12, 38-41 and 49-69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Despite applicant's amendment of claim 38 to recite that the "lineage committed human cells are differentiated to at least a point where they are programmed to develop only into a specific type of cell", the claims remain indefinite. Applicant's urgings regarding the insertion of "only" are taken to indicate that he wants to limit the cultured

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cells to those which are committed to a differentiation pathway the leads to only one type of differentiated cell. However, the examiner finds that the claims are not thus limited. For example, note the recitation of "leukocyte precursors" in claims 57 and 67; this leads to confusion, since a "leukocyte" is any type of white blood cell such as polymorphonuclear neutrophils, eosinophils, basophils, lymphocytes and monocytes (Cruse et al page 185). In other words, a "leukocyte precursor" has a multipotential capacity; it must lie somewhere toward the top of Figure 2-1 of Clark et al (of record).

Also, from viewing Figure 2-1 of Clark et al note that "monocytes" (recited in claims 57 and 59) do not represent a cell that is "programmed to develop only into a specific type of cell" since these form both macrophages and histocytes.

Additionally, one is confused by claim 69, which recites "at least one cell type selected from the group consisting of T-cells, B-cells, and mixtures thereof." A mixture of T-and B-cells clearly does not consist of lineage-committed cells "programmed to develop only into a specific type of cell".

One can carry this analysis even further. Are the "T-cells" of claim 69 "a specific type of cell" or not? It is known that, in T-cell development, early stage T-cells (Pre-T-cells) can be programmed along at least two paths of differentiation to form helper T-cells or cytotoxic/effector T-cells (See Clark at Fig. 2-1); these are now known as CD 4+ or CD8+ T-cells, respectively, both of which also express CD 3 surface molecules associated with the TCR (instant pg. 7). The CD4+ differentiate, along different paths to form Th0, Th1 or Th2 cells (Libeau et al). Given this complexity and the vague nature of applicant's disclosure one would not know whether cells "programmed to develop

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only into a specific type of cell would mean cells that develop to form all CD3+ T-cells, to form the subpopulation of CD3+ CD4+ helper T-cells, or to form the further subpopulation of Th0, Th1 or Th2 helpers.

Also note that claim 57 recites "at least one type of cell" (line 2) and "mixtures" thereof "(line 5)." "Mixtures" of more than "one type" of lineage committed cell are clearly not capable of being "programmed to develop only into a specific type of cell" as required by claim 38.

Claims 6-7, 10-12, 38-41 and 49-69 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Given the above noted confusion under 112, 2nd as what applicant is claiming, it is considered that applicant did not know what his invention was and did not adequately describe the invention.

Claim 69 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 69 contains new matter because page 7 does not support "mixtures" of T and B-cells.

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Given the above noted confusion regarding what it means for a cell to be "programmed to develop only into a specific type of cell" it is considered proper for the examiner to interpret the stromal cells and hematopoietic progenitor cells of the prior art references as being such cells. Therefore the prior art rejections of record are maintained as follows:

Claims 10-12, 38-40 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Emerson et al (, 437,994), for reasons of record.

Emerson et al teach culturing of stromal cells at cell densities and at rates of medium exchange (col. 6, lines 1-8) consistent with claim 38. Enhanced proliferation and secretion of GM-CSF are consistent with claims 39-40 and 49.

Claims 10, 12 and 38-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Caldwell et al (Jour. Cellular Physiol., 147, 244, 1991), for reasons of record.

Caldwell et al teach culturing of stromal cells at a cell density of ten to the fourth cells per ml, with a medium exchange schedule of 50% or 100% per day (page 345, col. 2). Enhanced GM-CSF secretion is consistent with claims 39-40 and 49.

Claims 10-12 and 38-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Emerson et al (5,437,994) for reasons of record.

See infra.

Claims 10-12 and 38-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Emerson et al (5,605,822 or 5,635,386 or 5,646,043 or 5,670,147 or 6,326,198) for reasons of record.

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Following the rationale set forth at pages 7-8 of the previous action it is deemed that "enhanced biological function" would have necessarily been a consequence of culturing hematopoietic progenitor cells at the taught cell densities and rates of medium exchange. Also, as noted at page 8 of the action the granulocyte – macrophage progenitors provide more effective reconstitution of line marrow, as is consistent with claim 39.

Applicant's urgings filed 5/24/04 have been considered but are unconvincing.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Saunders whose telephone number is (571) 272-

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0849. The examiner can normally be reached on Monday to Thursday from 8 AM to 5:30 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Saunders/LR
August 12, 2004

David A. Saunders
DAVID SAUNDERS
PRIMARY EXAMINER
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